A Tale of Two Outbreaks

David P. Dooley, M.D., FACP
COL, MC, USA

What has been, that will be;
What has been done, that will be done.
Nothing is new under the sun.

Even the thing of which we say, “See, this is new!” has already existed in the ages that preceded us.

– Ecclesiastes 1:9-11

There is no remembrance of the men of old;
nor of those to come will there be any

Outbreak Rules Reminder-I

1. **Verify Outbreak!**
   a. **Confirm diagnosis**
   b. Document that event is occurring at **greater frequency than expected over defined *time* and *place***
2. Consider immediate control measures
3. Develop case definition
4. Develop survey instrument
5. Develop hypothesis (-es)

Outbreak Rules Reminder-II

6. Assemble resources, team needed for investigation
7. Collect data. Describe time, person, place, exposures
8. Identify associations
9. Further control measures
10. Determine need for additional studies

Outbreak 1: Acute Eosinophilic Pneumonias, Iraq, 2003

- June 28 2003—1st query on email chain
  - f/u of pneumonia case A/Ed to Landstuhl out of Iraq
- Multiple emails next 2 days
  - Seeking diagnosis and f/u clarifications
  - Down command, epi/CHPPM, Army OTSG, Landstuhl, USAMRIID chains

Outbreak 1

- 1st patient—played volleyball up till day got sick; rapidly progressive respiratory failure
- Intubated, A/Eed to Landstuhl

- 30 June—3rd patient admitted. Alarms go off.
- Acc. to Landstuhl pulm docs—1-2 individuals/week with pneumonia since war; 1/month before war. 3 in LARMC ICU.

Outbreak 1--AEP

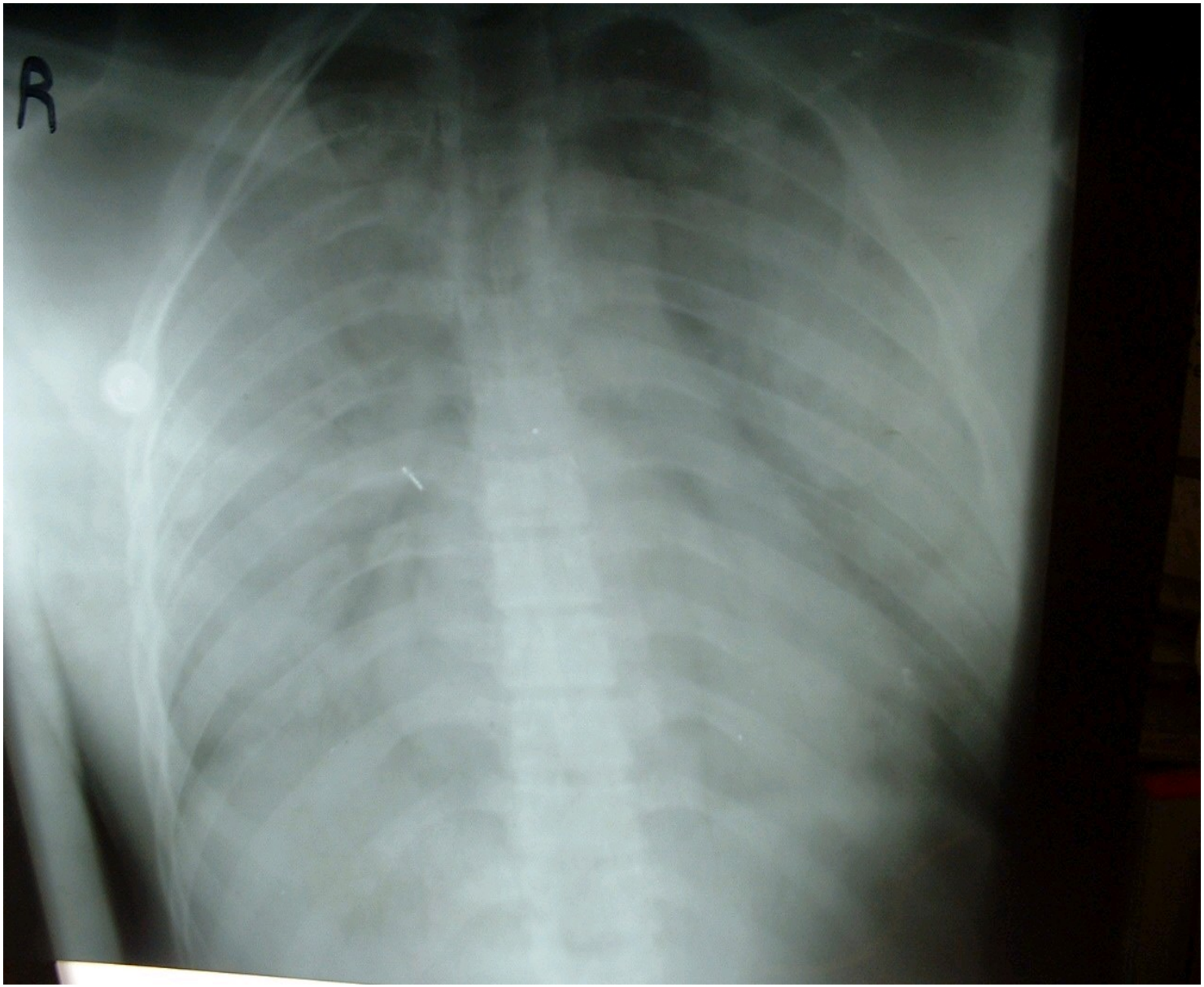
- Pathology/microbiology either negative, not obtained (far forward), or lost in chain
- 1st note from CHPPM June 28th: “?Is there a “Mysterious pneumonia outbreak’ going on over there?”
- 30 June: crescendo E-mails (0335, 1015, 1102, 1127, 1741, 0600 next day) asking for data

Outbreak 1--AEP

- July 2: PM observers in-country call for better data (Patient ID, demographics, exposures, etc.)
- Questionnaire developed/fielded by LTC Bybee (PM)
- Highly fragmented process. 2 in-country PM docs seize moment: interview, collect data, collate

Outbreak 1--AEP

- Early patient died during evacuation (arrest during transfer to helicopter)
- Early autopsy results (~1 July)—pulmonary edema; initial cultures negative


R

Outbreak 1--AEP

- 1st epi review available 1 July
  - 31 cases in country.
  - 1 died
  - 5 air-evacuated; rest recovered/RTD in theatre
  - Avg LOS 3.8 days
  - 2 unit “clusters” of only 2 each
  - MPs/engineers ? overrepresented (5 each)

Outbreak 1--AEP

- Arguments ensue over resources/assets for diagnostics
  - ID doc attached to TAML an 804th MED BDE asset, “not subject to V Corps C2”

Outbreak 1--AEP

- By 3 July, more complete autopsy results available
  - ARDS, pulm edema, DAD (diffuse alveolar damage)—final common pathway of injury
  - Pericardial/pleural effusions—probably aggressive fluid resuscitation

Outbreak 1--AEP

- 5 July---CJTF Surgeon notes that “providers on all levels have been educated on the clinical presentatons and suggested treatment and evacuation criteria”
- MEF, UK noted to have no cases (MEF one later)

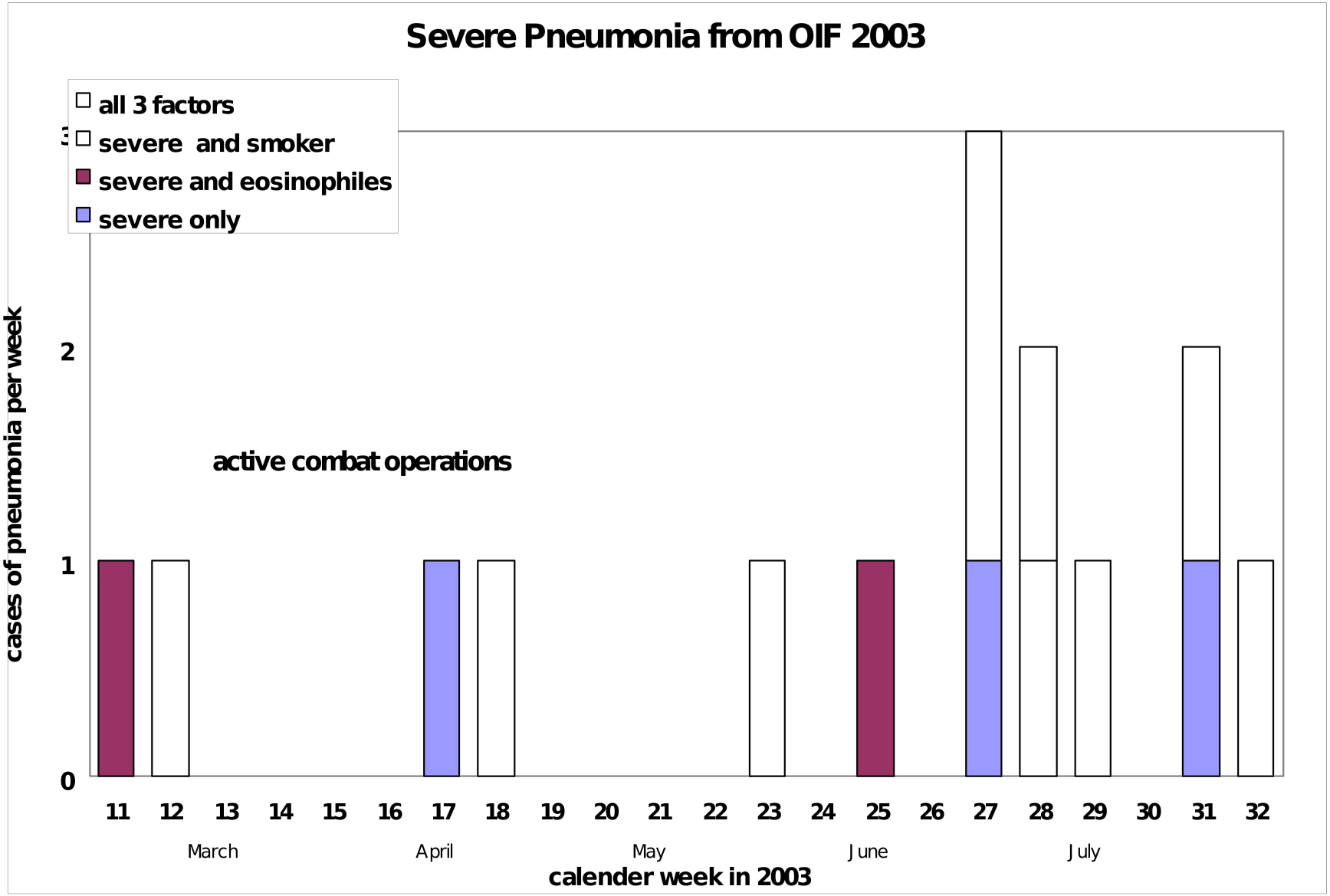
Outbreak 1--AEP

- LTC Milstrey (30th MED BDE PM consultant)—possessed huge database of epi data

- 6 July—Summary of cases at 28th CSH is produced
  - 9 cases; variety of exposures, severities, presentations, CXR changes, no commonality

Outbreak 1--AEP

- By 10 July:
  - Of 17 severe pneumonias
    - 10 intubated
    - 9/17 measured had eosinophilia (peripheral; 10-40%)
    - 2/17 with *S. pneumoniae* as isolated bacteria; others without etiology found
    - Smoking common, esp. new smokers


Severe Pneumonia from OIF 2003
all 3 factors
severe and smoker
severe and eosinophiles
severe only
cases of pneumonia per week
3
2
1
0
active combat operations
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
March
April
May
June
July
calender week in 2003

Outbreak 1--AEP

- Looking back, “…the ‘spike’ may have been a ‘blip’….’put on the brakes’”

- Epi team had been requested
- Then de-requested
- Still sent
  - Army SG spokesman answering CNN/Good Morning America interviews, accusations

Outbreak 1--AEP

- By end-July, diagnosed severe cases no longer recognized

- In retrospect,
  - About half of patients actively smoked (1/2 deaths)—roughly = background prevalence
  - 72% patients vaccinated against flu—75% of rest of population
  - 1:10,000 severe pneumonia cases = expected rate over this period

Outbreak 1--AEP

- Review of previous experience:
  - *Acute Eosinophilic Pneumonia* first recognized 14 years previously (Allen JN et al., NEJM 1989; expanded 1996, Pope-Harman AL et al, Medicine)
  - Described in military deployments (out of NTC; Degler and Giacoppe, Mil Med, 1999)

Outbreak 1--AEP

- Characterized by sudden onset of viral syndrome, cough (usually NP), SOB, respiratory insufficiency, and peripheral eosinophilia.

Outbreak 1--AEP

- Previous criteria:
  - Acute febrile illness of <5d duration, with respiratory failure;
  - Diffuse alveolar or mixed alveolar/interstitial CXR infiltrates;
  - BAL eosinophils > 25% (< half have peripheral too);
  - Absence of other infections;
  - Prompt, complete, nonrelapsing response to steroids

Outbreak 1--AEP

- Hypothesized to be acute hypersensitivity reaction to as yet unrecognized inhaled antigen

- Quandary in July, as now: how to diagnose early enough for steroids to work? Forward-based bronchoscopies difficult.

Outbreak 1--AEP

- Pertinent because:
- 23 January 2004—2 more soldiers admitted at LARMC with eosinophilic pneumonia (20 and 18%, respectively)

Outbreak 1—AEP Lessons Learned I

- Cool heads are good
  - Epi/PM guys stood back, took deep breaths, tackled the drudge work
- More forward-based diagnostics, the better

Outbreak 1—AEP Lessons Learned II

- Good to have scripted diagnosis/treatment guidelines published
- E-mail cuts both ways
  - Amazing speed of resolution of data
  - Amazing speed of elevation of non-outbreak to outbreak status, before cooler heads had chance to insert.

Outbreak 1--AEP

- How to handle the press:
  - Don’t lie
  - Don’t obfuscate
  - Don’t tell them any more that you absolutely have to
  - Don’t get angry when they make you look bad, it’s their job

Outbreak 2 *Acinetobacter* Wound Infections

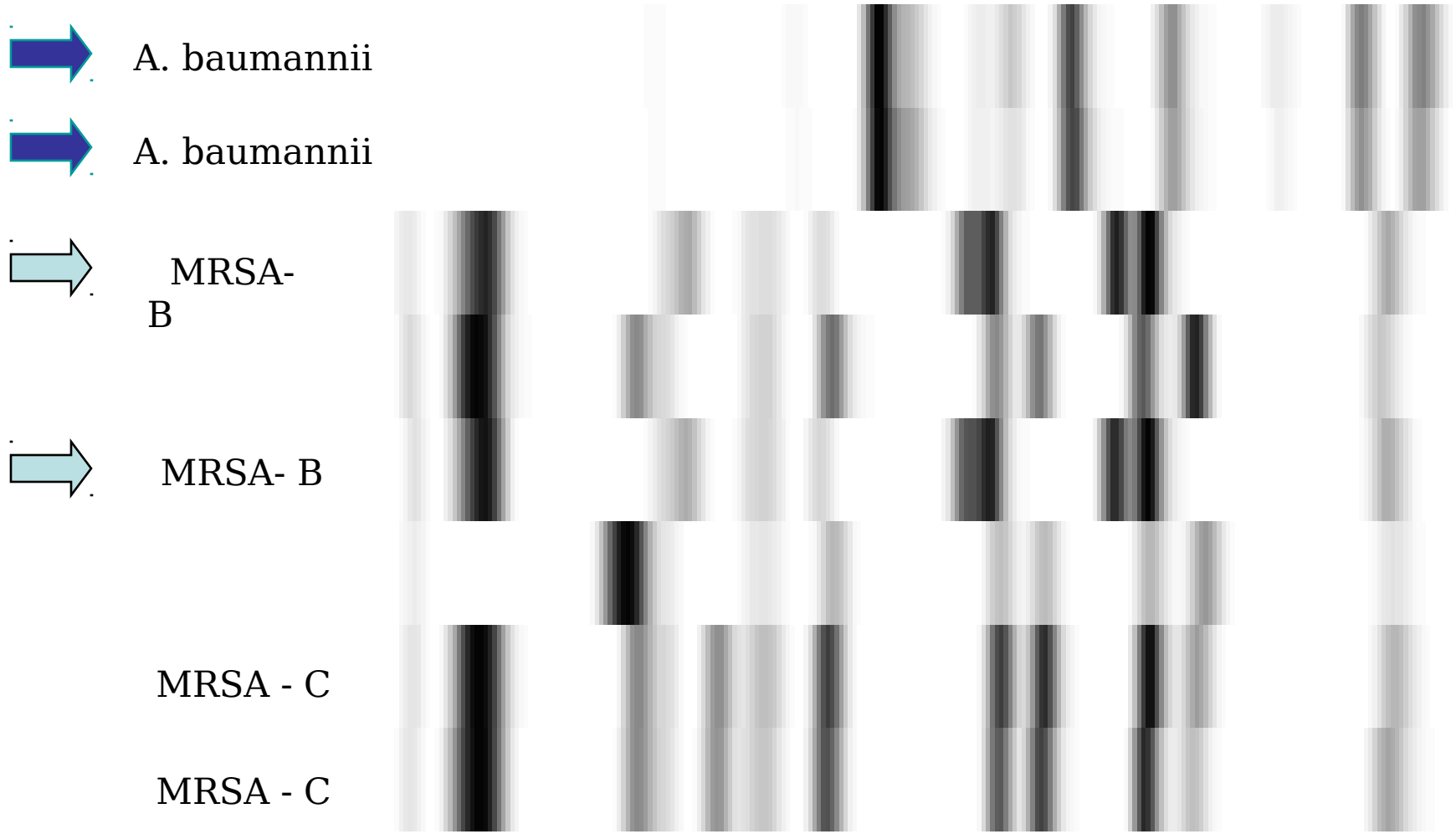
- April 2003
- Wounded are making way back through system in Iraq, then to USS Comfort or LARMC
- At both places, unusual number of wounds seem to be infected with *Acinetobacter baumanii*
- Raised above horizon because Comfort ran out of imipenem; Philadelphia depot sought permission to release

Acinetobacter baumannii

- Gram negative coccobacillus—looks like *Neisseria* or *Hemophilus*
- Ubiquitous in the environment
- Nosocomial infection in critical care settings
- Rare community-acquired infection in compromised patients
- Increasing drug resistance since 1970’s
- Most common phenotypes in US are highly resistant; seem to spread horizontally around hospitals

RiboPrinter® Grayscale of BAMC Isolat

Nosocomial Spread from Patient to Patient



USAISR

Outbreak 2 *Acinetobacter* Wound Infections

- Phone calls/emails go to experts
- Confirmed that this is hospital bug only
  - Comfort must have contaminated IV bags, ventilator tubings/solutions, etc.
- ?Why some of them seen before Comfort?
- ?Why some show up at LARMC, skip Comfort, with *Acinetobacter*?

Verify Presence of Outbreak

- Outbreak of *Acinetobacter baumannii* infections?
  - Definition: “…occurrence exceeds normal expectancy…”

Is this an Outbreak? Yes

- More than expected
  - 1-2% of wound infections in US hospitals
  - Not reported/recognized in Gulf War 1991
  - Exceeded WRAMC, LARMC, NNMC recent historical experience

Case Definition and Study Population

- Didn’t make sense. Epi investigation started.
- Case Definition
  - US military personnel injured or wounded in OIF with a positive *Acinetobacter baumannii* culture from any source
- Study population
  - 34 Operation Iraqi Freedom (OIF) casualties with *Acinetobacter* infections

Immediate Control Measures Instituted

- Environmental decontamination
- Isolate patients by infection/colonization status
- Establish separate initial evaluation and patient treatment areas
- Selective use of broad-spectrum antibiotics
- Hospital infection control practices (contact precautions) re-emphasized

Survey Instrument Developed

- Electronic Case Report Forms
  - Demographics
  - Clinical presentation and treatment provided
  - Evacuation sequence
  - Pre-infection antibiotic exposure
  - Antibiotic susceptibility of isolates
- Active case finding
  - Telephone
  - E-mail

Multidisciplinary Team

- Initial team
  - DoD-GEIS
  - Infectious Disease physician
  - Microbiologist
  - Preventive Medicine resident
- Expanded Team
  - Environmental scientist
  - Molecular biologist
  - Information technologist
  - Additional team members

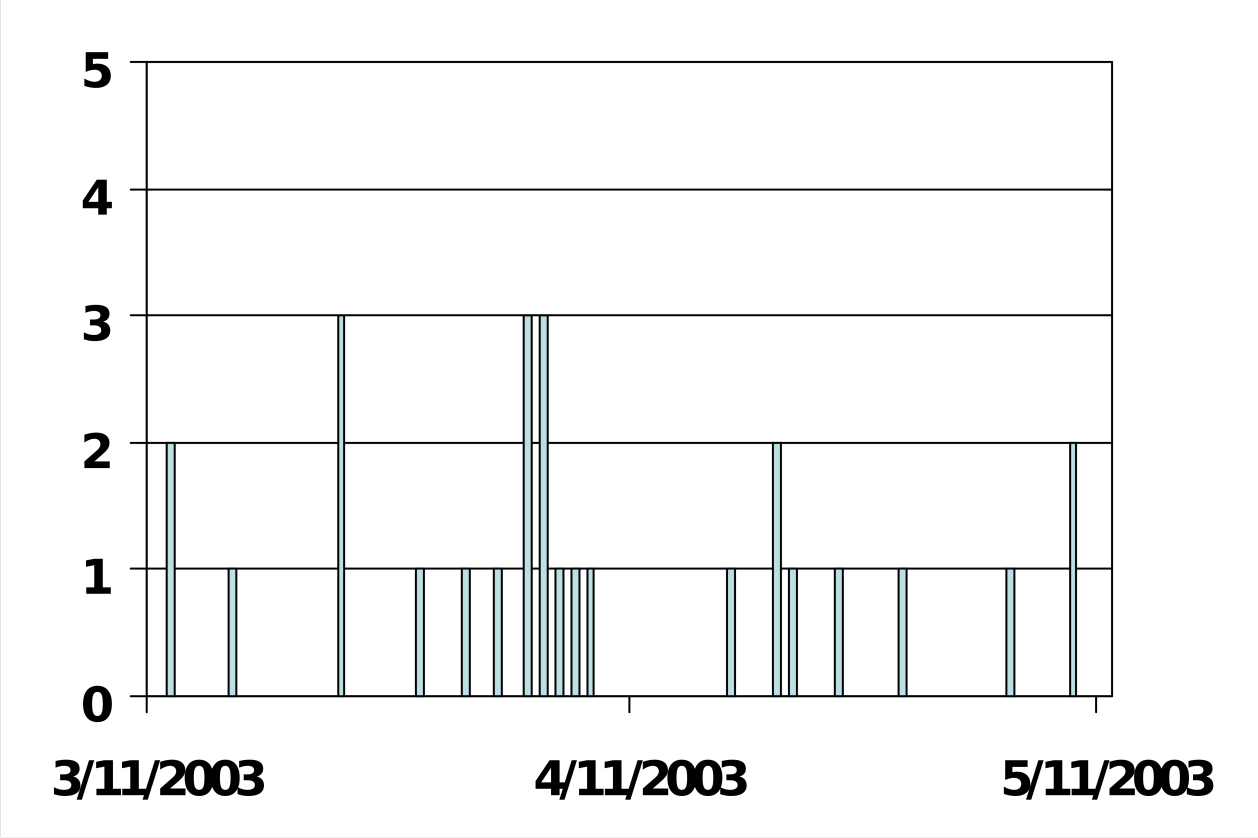
Hypotheses

- Survivor effect
- Source of infection
  - Environment
  - Nosocomial
- Antibiotic resistance

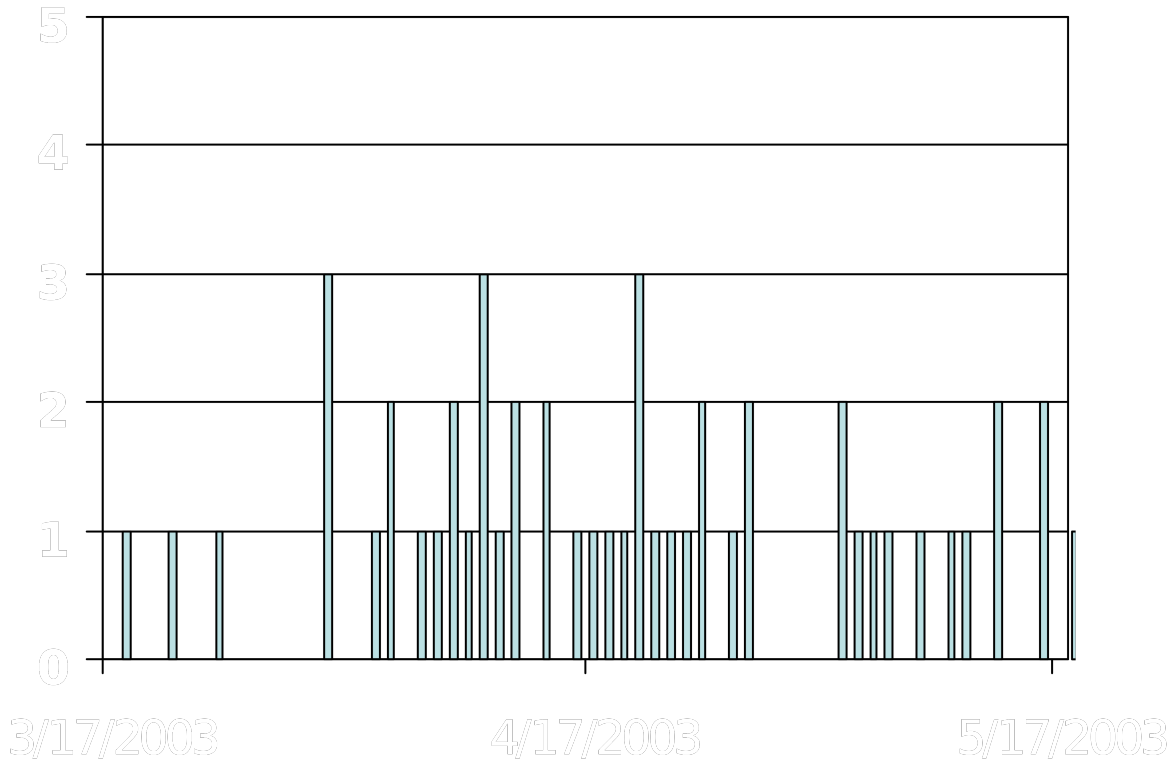
Location of Patients with *Acinetobacter* infections

MTF	N
Walter Reed	14
Landstuhl	11
National Naval	6
Brooke	3
Total	34

Casualty Epidemic Curve



Acinetobacter Culture Epidemic Curve



Sources of *Acinetobacter* Cultures

Culture site	**N**	**(%)**
Wound	32	(55)
Sputum	12	(20)
Tissue	6	(10)
Blood	4	(7)
Urine	2	(4)
Drain	1	(2)
Catheter tip	1	(2)
Total	58	(100)

Demographic of Cases

Characteristic		N	(%)
Sex	Male	32	(94)
	Female	2	(6)
Age (years)	18-20	2	(6)
	21-25	17	(50)
	26-35	9	(26)
	>35	4	(12)
Branch of Service	Army	15	(44)
	Marines	8	(24)
	Unknown	11	(32)

Geographic Location of Injury

		N (%)
Country	Kuwait	1 (3)
	Iraq (unknown)	33 (97)
Area of Operations	Forward	25 (73)
	Staging	4 (12)
	Support	1 (3)
	Unknown	4 (12)

Phenotype of *Acinetobacter* Isolates

Antibiotic susceptibility in vitro	**N (% total isolates)**
None	1 (2)
Carbapenem only	24 (41)
Carbapenem + one other drug class only	15 (26)
Other	18 (31)

N total isolates: 58

Identify Associations

- Traumatic Injury
  - Combat casualty
  - Accident
- Invasive Treatment
  - Surgical intervention
  - Invasive medical support
- Treatment at MTFs in-theater

Traumatic Wounds

- **Type of injury (%)**
  - Penetrating (55)
  - Fracture (50)
  - Crush (27)
  - Burn (3)
- **Location (%)**
  - Extremity (93)
  - Abdomen (30)
  - Head (27)
  - Chest (20)

Invasive Treatment Provided

- **Surgical Intervention (%)**
  - Wound I & D (61)
  - Laparotomy (39)
  - Fracture fixation (35)
  - Neurosurgical procedure (16)
  - Amputation (13)
- **Medical Support (%)**
  - Intubation/ventilation (55)
  - Urinary catheter (51)
  - Blood transfusion (29)
  - Chest tube (13)

Location Life/Limb-Saving Treatment Provided In-Theater

MTF	Number of Infections
47th CSH	11
67th CST	6
28th CSH	5
MTF-86	5
86th CSH	5
Udhari	4
21st CSH	1
Unknown	11

Preliminary Analysis Findings

- Mixed type outbreak
  - Common source (continuous)
    - Environment
  - Propagated
    - Nosocomial transmission not ruled out
- High levels of antibiotic resistance
- Unlikely a bioweapon
  - Multiple phenotypes
- Unlikely a point source
  - No single common exposure
  - Multiple phenotypes

Additional Findings

- No common accessible data source exists to conduct laboratory or clinical active or passive surveillance
- No tasking authority to conduct public health investigation

And then…

- Summer 2003---dust storm rises over Saudi Arabia
- Blows out over Persian Gulf; envelopes Comfort
- Morning after, Comfort ID physician and microbiologist run up to dust-coated gunwale
- Culture swabs taken: *Acinetobacter baumannii*

Outbreak 2
Acinetobacter Wound Infections

- On review, old hands knew this
  - 50% of wound infections in Vietnam*
  - 31% of hospital-acquired infections in earthquake victims in Turkey in 1991**

*** Tong MJ, JAMA 1972; ** Oncul O et al, J Hosp Infection 2002**

Still Unanswered Questions Feb 2004

- Source of infection
  - ***All*** "Community acquired" from environment at time of injury?
  - Nosocomial transmission? Probably very little
- Antibiotic resistance
  - Present in environment—few data on initial isolates, before antibiotics
  - Developed in response to antibiotic exposure

Additional Investigations

- Isolates genotyped: varied clones (non-identity)
- Data on medical treatment records for in-theater care and evacuation routes poorly evaluable
  - Unsure of when organism acquired
  - Difficult to define when colonized vs infected

Future Research

- Active surveillance of drug resistant organisms in regions of world where US personnel are likely to operate
- Develop and implement an electronic, laboratory-based surveillance system throughout the entire Military Health System

Lessons Learned

- With world-wide deployments, need understanding of typical environmental bacterial threats (e.g., not just exotic parasites)
- With current resources, world-wide data base could be/should be established
- Institutional memory must remain

Acknowledgements

- Initial presentation of this data: Paul Scott, M.D.; PM, WRAIR
- Data collection/analysis team: LTC Joel Fishbain, CDR Clara Witt, LTC(P) Bruno Petruccelli, COL Patrick Kelley, COL Robert DeFraites, Mr. Warren Wortman, Ms. Jackie Howard, Ms. Paula Gray